IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Turner Jr. *et al.* (As Previously Amended)		
Serial No.:	09/918,359	Group Art Unit:	1646
Filed:	07/30/2001	Examiner:	J. Murphy
For: Human Ion Channel Proteins and Polynucleotides Encoding the Same (As Previously Amended)		Attorney Docket No.:	LEX-0208-USA

APPEAL BRIEF

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Commissioner for Patents
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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on May 30, 2003. The Notice of Appeal was timely submitted on August 28, 2003, and was received in the Patent and Trademark Office ("the Office") on September 2, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of one month to and including December 2, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(1) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief ($165.00), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

The present application was filed on July 30, 2001, claiming the benefit of U.S. Provisional Application Numbers 60/221,643 and 60/222,503, which were filed on July 28, 2000 and August 2, 2000, respectively, and included original claims 1-6. A Restriction and Election Requirement was issued on August 28, 2002, separating the original claims into three separate and distinct inventions. In a response to the Restriction and Election Requirement submitted to the Office on September 23, 2002, Appellants elected without traverse to prosecute the claims of the Group III invention (original claims 1, 5 and 6) for prosecution on the merits, cancelled claims 2-4 without prejudice and without disclaimer as drawn to non-elected inventions, amended the inventorship and claims 1 and 6 to reflect the election of the Group III invention, amended claim 5 to further improve its clarity, and added new claims 7-9.

A First Official Action on the merits ("the First Action") was issued on December 13, 2002, in which the title of the application was objected to, claims 1 and 5-9 were rejected under 35 U.S.C. § 101 as allegedly lacking a patentable utility, claims 1 and 5-9 were rejected under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, claim 5 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claim 5 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, claim 5 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, and claim 5 was rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Adams *et al.* (EST Database Accession Number AA309878; "Adams"). In a response to the First Official Action submitted to the Office on March 12, 2003 ("Response to the First Action"), Appellants amended the title of the application, amended claim 5 to even further improve its clarity, and addressed the various rejections of claims 1 and 5-9.

A Second and Final Official Action ("the Final Action") was issued on May 30, 2003, indicating that the objection to the title and the rejections of claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at

the time the application was filed, had possession of the claimed invention, claim 5 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, and claim 5 under 35 U.S.C. § 102(b) as allegedly anticipated by Adams, had been overcome by the amendments and remarks submitted in the Response to the First Action, but maintaining the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. In a response to the Final Action submitted to the Office on August 28, 2003 ("Response to the Final Action"), Appellants again addressed the rejections of claims 1 and 5-9.

An Advisory Action ("the Advisory Action") was mailed on November 4, 2003, maintaining the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. Therefore, claims 1 and 5-9 are the subject of this appeal. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

As no amendments subsequent to the Final Action have been filed, Appellants believe that no outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode a novel protein that shares structural similarity with mammalian ion channel proteins (specification at page 2, lines 5-7).

The presently claimed polynucleotide sequences were compiled from clustered sequence from cDNA clones from a human brain cDNA library and products from human cerebellum mRNA (specification at page 15, lines 29-32). A number of coding single nucleotide polymorphisms were identified in the claimed sequence - specifically, an A/G transition at nucleotide position 271 of SEQ ID NO:6, which can result in an asparagine or glutamate being present at corresponding amino acid position

91 of SEQ ID NO:7; a C/G transversion at nucleotide position 364 of SEQ ID NO:6, which can result in an arginine or glycine being present at corresponding amino acid position 122 of SEQ ID NO:7; a G/A transition at nucleotide position 367 of SEQ ID NO:6, which can result in a glycine or serine being present at corresponding amino acid position 123 of SEQ ID NO:7; a T/A transversion at nucleotide position 699 of SEQ ID NO:6, which can result in a serine or asparagine being present at corresponding amino acid position 233 of SEQ ID NO:7; a T/C transition at nucleotide position 1013 of SEQ ID NO:6, which can result in an isoleucine or threonine being present at corresponding amino acid position 338 of SEQ ID NO:7; a G/A transition at nucleotide position 1015 of SEQ ID NO:6, which can result in an valine or methionine being present at corresponding amino acid position 339 of SEQ ID NO:7; a C/A transversion at nucleotide position 1397 of SEQ ID NO:6, which can result in a proline or histidine being present at corresponding amino acid position 466 of SEQ ID NO:7; a G/C transversion at nucleotide position 1405 of SEQ ID NO:6, which can result in an aspartate or histidine being present at corresponding amino acid position 469 of SEQ ID NO:7; and a G/T transition at nucleotide position 1419 of SEQ ID NO:6, which can result in a glutamate or aspartate being present at corresponding amino acid position 473 of SEQ ID NO:7 (specification from page 15, line 33 to page 16, line 32).

The specification details a number of uses for the presently claimed polynucleotide sequences, including in diagnostic assays such as forensic analysis (see, for example, the specification at page 10, lines 27-33), in the identification of coding sequence (see, for example, the specification at page 2, line 36), in mapping a unique gene to a particular chromosome (see, for example, the specification at page 3, line 2), and in assessing gene expression patterns, particularly using a high throughput "chip" format (see, for example, the specification at page 5, lines 35-37).

VI. ISSUES ON APPEAL

1. Do claims 1 and 5-9 lack a patentable utility?
2. Are claims 1 and 5-9 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, associated with the utility rejection, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 1 and 5-9 Lack a Patentable Utility?

The Final Action first rejects claims 1 and 5-9 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial or a well-established utility.

Appellants pointed out both in the Response to the First Action and the Response to the Final Action that the present nucleic acid sequences have utility in diagnostic assays, such as forensic analysis, as described in the specification as originally filed (see, for example, page 10, lines 27-33). As described in the specification from page 15, line 33 through page 16, line 32, the presently claimed sequence defines a number of coding single nucleotide polymorphisms - specifically, an A/G transition at nucleotide position 271 of SEQ ID NO:6, which can result in an asparagine or glutamate being present at corresponding amino acid position 91 of SEQ ID NO:7; a C/G transversion at nucleotide position 364 of SEQ ID NO:6, which can result in an arginine or glycine being present at corresponding amino acid position 122 of SEQ ID NO:7; a G/A transition at nucleotide position 367 of SEQ ID NO:6, which can result in a glycine or serine being present at corresponding amino acid position 123 of SEQ ID NO:7; a T/A transversion at nucleotide position 699 of SEQ ID NO:6, which can result in a serine or asparagine being present at corresponding amino acid position 233 of SEQ ID NO:7; a T/C transition at nucleotide position 1013 of SEQ ID NO:6, which can result in an isoleucine or threonine being present at corresponding amino acid position 338 of SEQ ID NO:7; a G/A transition at nucleotide position 1015 of SEQ ID NO:6, which can result in an valine or methionine being present at corresponding amino acid position 339 of SEQ ID NO:7; a C/A transversion at nucleotide position 1397 of SEQ ID NO:6, which can result in a proline or histidine being present at corresponding amino acid position 466 of SEQ ID NO:7; a G/C transversion at nucleotide position1405 of SEQ ID NO:6, which can result in an aspartate or histidine being present at corresponding amino acid position 469 of SEQ ID NO:7; and a G/T transition at nucleotide position 1419 of SEQ ID

NO:6, which can result in a glutamate or aspartate being present at corresponding amino acid position 473 of SEQ ID NO:7. As such polymorphisms are the basis for **forensic** analysis, which does not require any information at all about the ultimate biological function of the encoded protein, and that is undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful.

Appellants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to distinguish individual members of the human population from one another based simply on the presence or absence of one or more of the described polymorphisms. The skilled artisan would be able to use the presently described polymorphisms in forensic analysis exactly as they were described in the specification as originally filed, without **any** additional research. It is important to note that simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain these polymorphic markers does not mean that additional research is needed in order for these markers as they are presently described in the instant specification to be used in forensic science.

This is also not a case of a potential utility. Even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population). Appellants point out that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Appellants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Appellants respectfully point out that all that is required to support Appellants' assertion of utility is for the skilled artisan to believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion. Therefore, the presently claimed sequence clearly has a substantial and well established utility.

The Final Action questioned this asserted utility, stating "(s)uch assays can be performed with any

polynucleotide" (the Final Action at page 6). As set forth in the Response to the Final Action, this argument is flawed in a **number** of respects. First, Appellants submit that the asserted forensic utility is specific precisely because it cannot be applied to just any polynucleotide. In fact, the basis for forensic analysis is the fact that such polymorphic markers are **not** present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Second, until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is **meaningless**. The Examiner appears to be attempting to use the information presented for the first time by Appellants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such hindsight analysis based on Appellants discovery is completely improper. Third, the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. The fact that other polymorphic markers have been identified in other genetic loci, or that the use of the presently described polymorphic markers will provide additional information concerning the prevalence of these markers in certain subpopulations, does not mean that use of the polymorphic markers identified by Appellants' in SEQ ID NO:6 in forensic analysis is not a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

In other words, just because other (possibly better) polymorphic markers from the human genome have been described, or that additional information about the presently described polymorphic markers can be gained through the use of these markers, does not establish that the presently described polymorphic markers lack a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the

Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. In view of the above standards and "common sense" analysis, there can be little question that the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Appellants pointed out in the Response to the Final Action that the holding in the *Carl Zeiss* case is **mandatory legal authority** that essentially controls the outcome of the present case. This case, and particularly the cited quote, **directly** rebuts the Examiner's argument, which is presumably why the Examiner failed to address the holding of *Carl Zeiss* in the Final Action. In the Advisory Action, the Examiner attempts to distinguish the holding in *Carl Zeiss* from the present case, stating that "Carl Zeiss is inapposite to the facts of the instant case" because "(i)n the instant case, however, the claims lack utility not because they are incomplete, and not because they do not set forth the best or only way to accomplish a result, and not because that (sic) are not unique, but because they do not have either a well-established utility or a specific and substantial asserted utility" (the Advisory Action at page 2). The Examiner seems to believe that use of polymorphic markers in forensic analysis is not well-established because "the specification does not disclose the nexus between any of these polymorphisms and any function of the expressed polynucleotide" and "(t)here is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder" (the Advisory Action at page 2). Appellants respectfully point out that these arguments in no way

support the alleged lack of utility of the claimed sequence, but, rather, only serve to highlight the Examiner's general lack of understanding of forensic analysis. As repeatedly pointed out by Appellants, **forensic** analysis does not require **any** knowledge about "any function of the expressed polynucleotide" or a correlation "between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder". Forensic analysis is used to distinguish individual members of the human population from one another based simply on the presence or absence of one or more of the described polymorphisms. No more and no less is required. No knowledge about the function of the encoded protein is required. No nexus between the polymorphic markers and a specific disease or disorder is required. The present polymorphic markers clearly have utility in forensic analysis, and, thus, the claims meet the requirements of 35 U.S.C. § 101.

The Examiner further states that "Applicant further argues that the asserted utility is specific because it cannot be applied to any polynucleotide other than the one claimed" (the Advisory Action at page 2). This statement could not be any further from the truth. For the record, it is **not**, and **never** has been, Appellants position that the asserted utilities "cannot be applied to any polynucleotide other than the one claimed", but, rather, that these utilities can only be applied to a **subset** of nucleic acid sequences. Therefore, based on the fact that these utilities apply only to a subset of nucleic acid sequences, Appellants properly cite *Carl Zeiss* for the holding that "[A]n invention need not be the best or only way to accomplish a certain result" (*Carl Zeiss, supra*). The polymorphic markers described by Appellants do not need to be the best polymorphic markers, or the only polymorphic markers - they merely need to function as polymorphic markers, which is clearly the case. Thus, this argument also in no way supports the alleged lack of utility.

Furthermore, Appellants pointed out in the Response to the Final Action as the presently described polymorphisms are a part of the family of polymorphisms that have a well-established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis as described in the specification as originally filed, without the need for any further research. As discussed above, even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation

would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Again, as a matter of law, it is well settled that a patent need not disclose what is well known in the art (*In re Wands, supra*).

The Examiner attempts to distinguish the holding in *Brana* from the present case, stating that "Brana is inapposite to the facts of the instant case" because "(h)ere, the claims lack utility not because they are not ready for use as a drug, but because they do not have either a well-established utility or a specific and substantial asserted utility" (the Advisory Action at page 2). Once, again, as discussed in great detail, above, the Examiner seems to believe that use of polymorphic markers in forensic analysis is not well-established because "the specification does not disclose the nexus between any of these polymorphisms and any function of the expressed polynucleotide" and "(t)here is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder" (the Advisory Action at page 2). These statements completely mischaracterize forensic analysis, as fully detailed above, and therefore have no bearing whatsoever on Appellants assertion that the presently claimed sequence finds a patentable utility in forensic analysis. Appellants only wish to add at this point that the Examiner has provided absolutely **no** evidence of record that would serve to show that an artisan skilled in the art of forensic analysis would doubt Appellants asserted utility. As set forth by Appellants in the Response to the Final Action, it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As set forth in *In re Langer* (183 USPQ 288 (CCPA 1974); "*Langer*"):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as

> sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such **evidence** from the Examiner concerning the use of the presently described polymorphisms in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Additionally, in both the Response to the First Action and the Response to the Final Action, Appellants pointed out that a sequence sharing nearly 100% percent identity at the protein level over extended portions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and had been annotated by third party scientists *wholly unaffiliated with Appellants* as "Homo sapiens two-pore calcium channel protein 2" (GenBank accession number AY029200; alignment and GenBank report shown in **Exhibit A**). As set forth repeatedly by Appellants, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be no question that those skilled in the art would clearly believe that Appellants' sequence is an ion channel protein, exactly as asserted by Appellants in the specification as originally filed (at least at page 2, lines 5-7) . Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner questions this asserted utility, citing articles by Doerks *et al.* (Trends in Genetics *14*:248-250, 1998; "Doerks"), Brenner (TIG *15*:132-133, 1999; "Brenner"), and Bork *et al.* (Trends in Genetics *12*:425-427, 1996; "Bork") to support the argument that "the assignment of function based on homology is inherently difficult" (the Final Action at page 6). Appellants have addressed the shortcomings of each of these references in both the Response to the First Action and the Response to the Final Action, but neither the Final Action nor the Advisory Action provide any comments at all on Appellants' arguments. Therefore, Appellants will address the shortcomings of each of these references, and then address the argument of whether such articles support an alleged lack of patentable utility.

The Examiner cites Doerks for the proposition that sequence-to-function methods of assigning

protein function are prone to errors. However, Doerks *et al.* states that "utilization of family information and thus a more detailed characterization" should lead to "simplification of update procedures for the entire families if functional information becomes available for at least one member" (Doerks, page 248, paragraph bridging columns 1 and 2, emphasis added). Appellants point out that, as detailed above, a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Appellants* as a two-pore calcium channel protein (see **Exhibit A**). The two-pore ion channel superfamily is a well-studied protein family with a large amount of known functional information, exactly the situation that Doerks suggests will "simplify" and "avoid the pitfalls" of previous sequence-to-function methods of assigning protein function (Doerks, page 248, columns 1 and 2). Thus, instead of supporting the Examiner's position against utility, Doerks actually supports Appellants' position that the presently claimed sequences have a substantial and credible utility.

The Examiner cites Brenner as teaching that "most homologs must have different molecular and cellular functions" (the First Action at page 5). However, this statement is based on the assumption that "if there are only 1000 superfamilies in nature, then most homologs must have different molecular and cellular functions" (Brenner, page 132, second column). Furthermore, Brenner suggests that one of the main problems in using homology to predict function is "an issue solvable by appropriate use of modern and accurate sequence comparison procedures" (Brenner, page 132, second column), and in fact references an article by Altschul *et al.*, which is the basis for one of the "modern and accurate sequence comparison procedures" used by Appellants. Thus, the Brenner article also does not support the alleged lack of utility.

The Examiner finally cites Bork as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable, based on the "structural similarity of a small domain of the new protein to a small domain of a known protein" (the First Action at page 5). Thus, the Examiner's reliance on Bork has the same failing as described above for Doerks, specifically, the assumption that Appellants assertion that the present sequence is an ion channel protein is made on the basis of structural similarity of a small domain of the new protein to a small domain of a known protein.

Appellants once again point out that a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Appellants* as a two-pore calcium channel protein (see **Exhibit A**). Thus, Appellants assertion that the present sequence is an ion channel protein is not made on the basis of "structural similarity of a small domain of the new protein to a small domain of a known protein", but rather vast homology over large tracts of the sequence. Thus, Bork also does not support the alleged lack of utility for the present invention.

Thus, while Appellants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes an ion channel protein, the Examiner has provided no evidence that directly establishes that the specifically claimed sequence does not encode an ion channel protein. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility.

Furthermore, with regard to the citation of journal articles to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these articles are merely the latest examples. Appellants readily agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Appellants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is not the standard for patentability under 35 U.S.C. § 101. Appellants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be believable. Appellants submit that the overwhelming majority of those of skill in the relevant art would believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by hundreds if not

thousands of journal articles, and would thus believe that Appellants sequence is a calcium ion channel protein. As believability is the standard for meeting the utility requirement of 35 U.S.C. § 101, and not 100% consensus or 100% accuracy, Appellants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101.

The Examiner states that "since the polypeptide encoded by the instant nucleic acid is not 100% identical to the AY029200 polynucleotide, the function of the polypeptide encoded by the instant nucleic acid is still not known' (the Final Action at page 6). However, Appellants respectfully point out that the PTO itself does not require 100% identity between proteins to establish functional homology. Example 10 of the Revised Interim Utility Guidelines Training Materials (**Exhibit B**) only requires a similarity score greater than 95% to establish functional homology. Thus, scientific publications that generally assert that very small changes between amino acid sequences can lead to changes in function, or publications describing specific examples of proteins, distinct from Appellants sequence, where a minor change in amino acid sequence has lead to a change in function, have been viewed by the PTO itself as irrelevant to the question of utility, and thus do not support the Examiner's allegation that the presently claimed sequence lacks utility. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

The Final Action and the Advisory Action additionally state that "(s)ince the AY029200 polynucleotide is a post-filing reference, the asserted utility was not well-established at the time of filing" (the Final Action at page 6 and the Advisory Action at page 2). Appellants respectfully pointed out in the Response to the Final Action that this argument is completely irrelevant to the utility issue at question here. Appellants pointed out that the utility of the presently claimed sequence as an ion channel protein was clearly asserted in the specification as originally filed, which is **all** that is required under 35 U.S.C. § 101. That others later confirm Appellants asserted utility to be true does not mean that the utility as originally asserted does not meet the requirements of 35 U.S.C. § 101.

Although Appellants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657

(Bd. Pat. App. & Inter. 1988)), in both the Response to the First Action and the Response to the Final Action, Appellants detailed an additional example of the utility of the present nucleotide sequences, as described in the specification at page 5, lines 35-37, specifically that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit** ℂ), 5,556,752 (**Exhibit** 𝔻), 5,744,305 (**Exhibit** 𝔼), 5,837,832 (**Exhibit** 𝔽), 6,156,501 (**Exhibit** 𝔾) and 6,261,776 (**Exhibit** ℍ). Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies that have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section VIII(B), below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questioned this asserted utility, stating that "all nucleic acids and genes are

in some combination useful in polynucleotide arrays" (the Final Action at page 7). Appellants point out that the Examiner once again is clearly confusing the requirements of a specific utility with a unique utility. Simply because other polynucleotide sequences can be used to track gene expression on a gene chip does not mean that the use of the presently claimed nucleic acid sequence in gene chip applications is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Therefore, this argument also fails to support the alleged lack of utility of the presently claimed compositions.

Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit I**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit J**. Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As yet a further example of the utility of the presently claimed polynucleotide, Appellants noted in the Response to the First Action and the Response to the Final Action that the present nucleotide sequence has a specific utility in "identification of coding sequence" (specification at page 2, lines 34-36) and in "determining the genomic structure" of the protein encoding regions of the corresponding human chromosome (specification at page 10, line 32). This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11 (present within the chromosome 11 clone presented in GenBank Accession Number AP003071; alignment and the first page from the GenBank report are presented in **Exhibit K**). Appellants respectfully remind the Board that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence

defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). It is well known that intron/exon boundaries are mutational hot spots, and thus the identification of the actual splice sites is of great utility to the skilled artisan. Such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone, and, as detailed in the specification, at least from page 10, line 33 to page 11, line 2, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Appellants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

As an additional example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 3, line 2, the present nucleotide sequences have a specific utility in "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11, as detailed above (**Exhibit K**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325; **Exhibit I**, which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter

et al. article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questions these asserted utilities, stating that "(s)uch assays can be performed with any polynucleotide" (the Final Action at page 7). This argument is flawed in a number of respects. First, Appellants point out that only a small number of other nucleotide sequences can be used to map the protein coding regions in this specific region of chromosome 11. Thus, this analysis can **not** "be performed with any polynucleotide". Second, the Examiner once again is clearly confusing the requirements of a **specific** utility with a **unique** utility. The fact that a small number of other nucleotide sequences could be used to map the protein coding regions in this specific region of chromosome 11 does not mean that the use of Appellants' sequence to map the protein coding regions of chromosome 11 is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

Regarding the utility requirements under 35 U.S.C. § 101, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)). Thus, based on the relevant case law, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, While Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent

examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit L**), 5,654,173 (**Exhibit M**), and 5,552,281 (**Exhibit N**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit O**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants understand that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1 and 5-9 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in Section VIII(A) concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have

determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1 and 5-9 have been shown to have "a specific, substantial, and credible utility", as detailed in Section VIII(A) above, the present rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:7.

5. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence of SEQ ID NO:7; and

(b) hybridizes to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. (Previously Presented) An isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:6.

7. (Previously Presented) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

8. (Previously Presented) The recombinant expression vector of claim 7, wherein said isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:6.

9. (Previously Presented) A host cell comprising the recombinant expression vector of claim 7.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1 and 5-9 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

December 2, 2003
Date

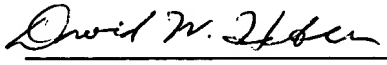

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TABLE OF AUTHORITIES

CASES

STATUTES

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Turner Jr. *et al.* (As Previously Amended)		
Serial No.:	09/918,359	Group Art Unit:	1646
Filed:	07/30/2001	Examiner:	J. Murphy
For:	Human Ion Channel Proteins and Polynucleotides Encoding the Same (As Previously Amended)	Attorney Docket No.:	LEX-0208-USA

APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on May 30, 2003. The Notice of Appeal was timely submitted on August 28, 2003, and was received in the Patent and Trademark Office ("the Office") on September 2, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of one month to and including December 2, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(1) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief ($165.00), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

The present application was filed on July 30, 2001, claiming the benefit of U.S. Provisional Application Numbers 60/221,643 and 60/222,503, which were filed on July 28, 2000 and August 2, 2000, respectively, and included original claims 1-6. A Restriction and Election Requirement was issued on August 28, 2002, separating the original claims into three separate and distinct inventions. In a response to the Restriction and Election Requirement submitted to the Office on September 23, 2002, Appellants elected without traverse to prosecute the claims of the Group III invention (original claims 1, 5 and 6) for prosecution on the merits, cancelled claims 2-4 without prejudice and without disclaimer as drawn to non-elected inventions, amended the inventorship and claims 1 and 6 to reflect the election of the Group III invention, amended claim 5 to further improve its clarity, and added new claims 7-9.

A First Official Action on the merits ("the First Action") was issued on December 13, 2002, in which the title of the application was objected to, claims 1 and 5-9 were rejected under 35 U.S.C. § 101 as allegedly lacking a patentable utility, claims 1 and 5-9 were rejected under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, claim 5 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claim 5 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, claim 5 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, and claim 5 was rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Adams *et al.* (EST Database Accession Number AA309878; "Adams"). In a response to the First Official Action submitted to the Office on March 12, 2003 ("Response to the First Action"), Appellants amended the title of the application, amended claim 5 to even further improve its clarity, and addressed the various rejections of claims 1 and 5-9.

A Second and Final Official Action ("the Final Action") was issued on May 30, 2003, indicating that the objection to the title and the rejections of claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled, claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at

the time the application was filed, had possession of the claimed invention, claim 5 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, and claim 5 under 35 U.S.C. § 102(b) as allegedly anticipated by Adams, had been overcome by the amendments and remarks submitted in the Response to the First Action, but maintaining the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. In a response to the Final Action submitted to the Office on August 28, 2003 ("Response to the Final Action"), Appellants again addressed the rejections of claims 1 and 5-9.

An Advisory Action ("the Advisory Action") was mailed on November 4, 2003, maintaining the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. Therefore, claims 1 and 5-9 are the subject of this appeal. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

As no amendments subsequent to the Final Action have been filed, Appellants believe that no outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode a novel protein that shares structural similarity with mammalian ion channel proteins (specification at page 2, lines 5-7).

The presently claimed polynucleotide sequences were compiled from clustered sequence from cDNA clones from a human brain cDNA library and products from human cerebellum mRNA (specification at page 15, lines 29-32). A number of coding single nucleotide polymorphisms were identified in the claimed sequence - specifically, an A/G transition at nucleotide position 271 of SEQ ID NO:6, which can result in an asparagine or glutamate being present at corresponding amino acid position

91 of SEQ ID NO:7; a C/G transversion at nucleotide position 364 of SEQ ID NO:6, which can result in an arginine or glycine being present at corresponding amino acid position 122 of SEQ ID NO:7; a G/A transition at nucleotide position 367 of SEQ ID NO:6, which can result in a glycine or serine being present at corresponding amino acid position 123 of SEQ ID NO:7; a T/A transversion at nucleotide position 699 of SEQ ID NO:6, which can result in a serine or asparagine being present at corresponding amino acid position 233 of SEQ ID NO:7; a T/C transition at nucleotide position 1013 of SEQ ID NO:6, which can result in an isoleucine or threonine being present at corresponding amino acid position 338 of SEQ ID NO:7; a G/A transition at nucleotide position 1015 of SEQ ID NO:6, which can result in an valine or methionine being present at corresponding amino acid position 339 of SEQ ID NO:7; a C/A transversion at nucleotide position 1397 of SEQ ID NO:6, which can result in a proline or histidine being present at corresponding amino acid position 466 of SEQ ID NO:7; a G/C transversion at nucleotide position1405 of SEQ ID NO:6, which can result in an aspartate or histidine being present at corresponding amino acid position 469 of SEQ ID NO:7; and a G/T transition at nucleotide position 1419 of SEQ ID NO:6, which can result in a glutamate or aspartate being present at corresponding amino acid position 473 of SEQ ID NO:7 (specification from page 15, line 33 to page 16, line 32).

The specification details a number of uses for the presently claimed polynucleotide sequences, including in diagnostic assays such as forensic analysis (see, for example, the specification at page 10, lines 27-33), in the identification of coding sequence (see, for example, the specification at page 2, line 36), in mapping a unique gene to a particular chromosome (see, for example, the specification at page 3, line 2), and in assessing gene expression patterns, particularly using a high throughput "chip" format (see, for example, the specification at page 5, lines 35-37).

VI. ISSUES ON APPEAL

1. Do claims 1 and 5-9 lack a patentable utility?
2. Are claims 1 and 5-9 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, associated with the utility rejection, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 1 and 5-9 Lack a Patentable Utility?

The Final Action first rejects claims 1 and 5-9 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial or a well-established utility.

Appellants pointed out both in the Response to the First Action and the Response to the Final Action that the present nucleic acid sequences have utility in diagnostic assays, such as forensic analysis, as described in the specification as originally filed (see, for example, page 10, lines 27-33). As described in the specification from page 15, line 33 through page 16, line 32, the presently claimed sequence defines a number of coding single nucleotide polymorphisms - specifically, an A/G transition at nucleotide position 271 of SEQ ID NO:6, which can result in an asparagine or glutamate being present at corresponding amino acid position 91 of SEQ ID NO:7; a C/G transversion at nucleotide position 364 of SEQ ID NO:6, which can result in an arginine or glycine being present at corresponding amino acid position 122 of SEQ ID NO:7; a G/A transition at nucleotide position 367 of SEQ ID NO:6, which can result in a glycine or serine being present at corresponding amino acid position 123 of SEQ ID NO:7; a T/A transversion at nucleotide position 699 of SEQ ID NO:6, which can result in a serine or asparagine being present at corresponding amino acid position 233 of SEQ ID NO:7; a T/C transition at nucleotide position 1013 of SEQ ID NO:6, which can result in an isoleucine or threonine being present at corresponding amino acid position 338 of SEQ ID NO:7; a G/A transition at nucleotide position 1015 of SEQ ID NO:6, which can result in an valine or methionine being present at corresponding amino acid position 339 of SEQ ID NO:7; a C/A transversion at nucleotide position 1397 of SEQ ID NO:6, which can result in a proline or histidine being present at corresponding amino acid position 466 of SEQ ID NO:7; a G/C transversion at nucleotide position1405 of SEQ ID NO:6, which can result in an aspartate or histidine being present at corresponding amino acid position 469 of SEQ ID NO:7; and a G/T transition at nucleotide position 1419 of SEQ ID

NO:6, which can result in a glutamate or aspartate being present at corresponding amino acid position 473 of SEQ ID NO:7. As such polymorphisms are the basis for **forensic** analysis, which does not require any information at all about the ultimate biological function of the encoded protein, and that is undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful.

Appellants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to distinguish individual members of the human population from one another based simply on the presence or absence of one or more of the described polymorphisms. The skilled artisan would be able to use the presently described polymorphisms in forensic analysis exactly as they were described in the specification as originally filed, without **any** additional research. It is important to note that simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain these polymorphic markers does not mean that additional research is needed in order for these markers as they are presently described in the instant specification to be used in forensic science.

This is also not a case of a potential utility. Even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population). Appellants point out that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Appellants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Appellants respectfully point out that all that is required to support Appellants' assertion of utility is for the skilled artisan to believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion. Therefore, the presently claimed sequence clearly has a substantial and well established utility.

The Final Action questioned this asserted utility, stating "(s)uch assays can be performed with any

polynucleotide" (the Final Action at page 6). As set forth in the Response to the Final Action, this argument is flawed in a **number** of respects. First, Appellants submit that the asserted forensic utility is specific precisely because it cannot be applied to just any polynucleotide. In fact, the basis for forensic analysis is the fact that such polymorphic markers are **not** present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Second, until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is **meaningless**. The Examiner appears to be attempting to use the information presented for the first time by Appellants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such hindsight analysis based on Appellants discovery is completely improper. Third, the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. The fact that other polymorphic markers have been identified in other genetic loci, or that the use of the presently described polymorphic markers will provide additional information concerning the prevalence of these markers in certain subpopulations, does not mean that use of the polymorphic markers identified by Appellants' in SEQ ID NO:6 in forensic analysis is not a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

In other words, just because other (possibly better) polymorphic markers from the human genome have been described, or that additional information about the presently described polymorphic markers can be gained through the use of these markers, does not establish that the presently described polymorphic markers lack a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the

Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. In view of the above standards and "common sense" analysis, there can be little question that the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Appellants pointed out in the Response to the Final Action that the holding in the *Carl Zeiss* case is **mandatory legal authority** that essentially controls the outcome of the present case. This case, and particularly the cited quote, **directly** rebuts the Examiner's argument, which is presumably why the Examiner failed to address the holding of *Carl Zeiss* in the Final Action. In the Advisory Action, the Examiner attempts to distinguish the holding in *Carl Zeiss* from the present case, stating that "Carl Zeiss is inapposite to the facts of the instant case" because "(i)n the instant case, however, the claims lack utility not because they are incomplete, and not because they do not set forth the best or only way to accomplish a result, and not because that (sic) are not unique, but because they do not have either a well-established utility or a specific and substantial asserted utility" (the Advisory Action at page 2). The Examiner seems to believe that use of polymorphic markers in forensic analysis is not well-established because "the specification does not disclose the nexus between any of these polymorphisms and any function of the expressed polynucleotide" and "(t)here is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder" (the Advisory Action at page 2). Appellants respectfully point out that these arguments in no way

support the alleged lack of utility of the claimed sequence, but, rather, only serve to highlight the Examiner's general lack of understanding of forensic analysis. As repeatedly pointed out by Appellants, **forensic** analysis does not require **any** knowledge about "any function of the expressed polynucleotide" or a correlation "between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder". Forensic analysis is used to distinguish individual members of the human population from one another based simply on the presence or absence of one or more of the described polymorphisms. No more and no less is required. No knowledge about the function of the encoded protein is required. No nexus between the polymorphic markers and a specific disease or disorder is required. The present polymorphic markers clearly have utility in forensic analysis, and, thus, the claims meet the requirements of 35 U.S.C. § 101.

The Examiner further states that "Applicant further argues that the asserted utility is specific because it cannot be applied to any polynucleotide other than the one claimed" (the Advisory Action at page 2). This statement could not be any further from the truth. For the record, it is **not**, and **never** has been, Appellants position that the asserted utilities "cannot be applied to any polynucleotide other than the one claimed", but, rather, that these utilities can only be applied to a **subset** of nucleic acid sequences. Therefore, based on the fact that these utilities apply only to a subset of nucleic acid sequences, Appellants properly cite *Carl Zeiss* for the holding that "[A]n invention need not be the best or only way to accomplish a certain result" (*Carl Zeiss, supra*). The polymorphic markers described by Appellants do not need to be the best polymorphic markers, or the only polymorphic markers - they merely need to function as polymorphic markers, which is clearly the case. Thus, this argument also in no way supports the alleged lack of utility.

Furthermore, Appellants pointed out in the Response to the Final Action as the presently described polymorphisms are a part of the family of polymorphisms that have a well-established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis as described in the specification as originally filed, without the need for any further research. As discussed above, even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation

would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Again, as a matter of law, it is well settled that a patent need not disclose what is well known in the art (*In re Wands, supra*).

The Examiner attempts to distinguish the holding in *Brana* from the present case, stating that "Brana is inapposite to the facts of the instant case" because "(h)ere, the claims lack utility not because they are not ready for use as a drug, but because they do not have either a well-established utility or a specific and substantial asserted utility" (the Advisory Action at page 2). Once, again, as discussed in great detail, above, the Examiner seems to believe that use of polymorphic markers in forensic analysis is not well-established because "the specification does not disclose the nexus between any of these polymorphisms and any function of the expressed polynucleotide" and "(t)here is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder" (the Advisory Action at page 2). These statements completely mischaracterize forensic analysis, as fully detailed above, and therefore have no bearing whatsoever on Appellants assertion that the presently claimed sequence finds a patentable utility in forensic analysis. Appellants only wish to add at this point that the Examiner has provided absolutely **no** evidence of record that would serve to show that an artisan skilled in the art of forensic analysis would doubt Appellants asserted utility. As set forth by Appellants in the Response to the Final Action, it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As set forth in *In re Langer* (183 USPQ 288 (CCPA 1974); "*Langer*"):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as

> sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such **evidence** from the Examiner concerning the use of the presently described polymorphisms in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Additionally, in both the Response to the First Action and the Response to the Final Action, Appellants pointed out that a sequence sharing nearly 100% percent identity at the protein level over extended portions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and had been annotated by third party scientists *wholly unaffiliated with Appellants* as "Homo sapiens two-pore calcium channel protein 2" (GenBank accession number AY029200; alignment and GenBank report shown in **Exhibit A**). As set forth repeatedly by Appellants, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be no question that those skilled in the art would clearly believe that Appellants' sequence is an ion channel protein, exactly as asserted by Appellants in the specification as originally filed (at least at page 2, lines 5-7) . Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner questions this asserted utility, citing articles by Doerks *et al.* (Trends in Genetics *14*:248-250, 1998; "Doerks"), Brenner (TIG *15*:132-133, 1999; "Brenner"), and Bork *et al.* (Trends in Genetics *12*:425-427, 1996; "Bork") to support the argument that "the assignment of function based on homology is inherently difficult" (the Final Action at page 6). Appellants have addressed the shortcomings of each of these references in both the Response to the First Action and the Response to the Final Action, but neither the Final Action nor the Advisory Action provide any comments at all on Appellants' arguments. Therefore, Appellants will address the shortcomings of each of these references, and then address the argument of whether such articles support an alleged lack of patentable utility.

The Examiner cites Doerks for the proposition that sequence-to-function methods of assigning

protein function are prone to errors. However, Doerks *et al.* states that "utilization of family information and thus a more detailed characterization" should lead to "simplification of update procedures for the entire families if functional information becomes available for at least one member" (Doerks, page 248, paragraph bridging columns 1 and 2, emphasis added). Appellants point out that, as detailed above, a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Appellants* as a two-pore calcium channel protein (see **Exhibit A**). The two-pore ion channel superfamily is a well-studied protein family with a large amount of known functional information, exactly the situation that Doerks suggests will "simplify" and "avoid the pitfalls" of previous sequence-to-function methods of assigning protein function (Doerks, page 248, columns 1 and 2). Thus, instead of supporting the Examiner's position against utility, Doerks actually supports Appellants' position that the presently claimed sequences have a substantial and credible utility.

The Examiner cites Brenner as teaching that "most homologs must have different molecular and cellular functions" (the First Action at page 5). However, this statement is based on the assumption that "if there are only 1000 superfamilies in nature, then most homologs must have different molecular and cellular functions" (Brenner, page 132, second column). Furthermore, Brenner suggests that one of the main problems in using homology to predict function is "an issue solvable by appropriate use of modern and accurate sequence comparison procedures" (Brenner, page 132, second column), and in fact references an article by Altschul *et al.*, which is the basis for one of the "modern and accurate sequence comparison procedures" used by Appellants. Thus, the Brenner article also does not support the alleged lack of utility.

The Examiner finally cites Bork as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable, based on the "structural similarity of a small domain of the new protein to a small domain of a known protein" (the First Action at page 5). Thus, the Examiner's reliance on Bork has the same failing as described above for Doerks, specifically, the assumption that Appellants assertion that the present sequence is an ion channel protein is made on the basis of structural similarity of a small domain of the new protein to a small domain of a known protein.

Appellants once again point out that a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Appellants* as a two-pore calcium channel protein (see **Exhibit A**). Thus, Appellants assertion that the present sequence is an ion channel protein is not made on the basis of "structural similarity of a small domain of the new protein to a small domain of a known protein", but rather vast homology over large tracts of the sequence. Thus, Bork also does not support the alleged lack of utility for the present invention.

Thus, while Appellants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes an ion channel protein, the Examiner has provided no evidence that directly establishes that the specifically claimed sequence does not encode an ion channel protein. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility.

Furthermore, with regard to the citation of journal articles to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these articles are merely the latest examples. Appellants readily agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Appellants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is not the standard for patentability under 35 U.S.C. § 101. Appellants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be believable. Appellants submit that the overwhelming majority of those of skill in the relevant art would believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by hundreds if not

thousands of journal articles, and would thus believe that Appellants sequence is a calcium ion channel protein. As believability is the standard for meeting the utility requirement of 35 U.S.C. § 101, and not 100% consensus or 100% accuracy, Appellants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101.

The Examiner states that "since the polypeptide encoded by the instant nucleic acid is not 100% identical to the AY029200 polynucleotide, the function of the polypeptide encoded by the instant nucleic acid is still not known' (the Final Action at page 6). However, Appellants respectfully point out that the PTO itself does not require 100% identity between proteins to establish functional homology. Example 10 of the Revised Interim Utility Guidelines Training Materials (**Exhibit B**) only requires a similarity score greater than 95% to establish functional homology. Thus, scientific publications that generally assert that very small changes between amino acid sequences can lead to changes in function, or publications describing specific examples of proteins, distinct from Appellants sequence, where a minor change in amino acid sequence has lead to a change in function, have been viewed by the PTO itself as irrelevant to the question of utility, and thus do not support the Examiner's allegation that the presently claimed sequence lacks utility. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

The Final Action and the Advisory Action additionally state that "(s)ince the AY029200 polynucleotide is a post-filing reference, the asserted utility was not well-established at the time of filing" (the Final Action at page 6 and the Advisory Action at page 2). Appellants respectfully pointed out in the Response to the Final Action that this argument is completely irrelevant to the utility issue at question here. Appellants pointed out that the utility of the presently claimed sequence as an ion channel protein was clearly asserted in the specification as originally filed, which is **all** that is required under 35 U.S.C. § 101. That others later confirm Appellants asserted utility to be true does not mean that the utility as originally asserted does not meet the requirements of 35 U.S.C. § 101.

Although Appellants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657

(Bd. Pat. App. & Inter. 1988)), in both the Response to the First Action and the Response to the Final Action, Appellants detailed an additional example of the utility of the present nucleotide sequences, as described in the specification at page 5, lines 35-37, specifically that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit C**), 5,556,752 (**Exhibit D**), 5,744,305 (**Exhibit E**), 5,837,832 (**Exhibit F**), 6,156,501 (**Exhibit G**) and 6,261,776 (**Exhibit H**). Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies that have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section VIII(B), below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questioned this asserted utility, stating that "all nucleic acids and genes are

in some combination useful in polynucleotide arrays" (the Final Action at page 7). Appellants point out that the Examiner once again is clearly confusing the requirements of a **specific** utility with a **unique** utility. Simply because other polynucleotide sequences can be used to track gene expression on a gene chip does not mean that the use of the presently claimed nucleic acid sequence in gene chip applications is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Therefore, this argument also fails to support the alleged lack of utility of the presently claimed compositions.

Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit I**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit J**. Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As yet a further example of the utility of the presently claimed polynucleotide, Appellants noted in the Response to the First Action and the Response to the Final Action that the present nucleotide sequence has a specific utility in "identification of coding sequence" (specification at page 2, lines 34-36) and in "determining the genomic structure" of the protein encoding regions of the corresponding human chromosome (specification at page 10, line 32). This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11 (present within the chromosome 11 clone presented in GenBank Accession Number AP003071; alignment and the first page from the GenBank report are presented in **Exhibit K**). Appellants respectfully remind the Board that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence

defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). It is well known that intron/exon boundaries are mutational hot spots, and thus the identification of the actual splice sites is of great utility to the skilled artisan. Such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone, and, as detailed in the specification, at least from page 10, line 33 to page 11, line 2, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Appellants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

As an additional example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 3, line 2, the present nucleotide sequences have a specific utility in "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11, as detailed above (**Exhibit K**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325; **Exhibit L**, which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter

et al. article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questions these asserted utilities, stating that "(s)uch assays can be performed with any polynucleotide" (the Final Action at page 7). This argument is flawed in a number of respects. First, Appellants point out that only a small number of other nucleotide sequences can be used to map the protein coding regions in this specific region of chromosome 11. Thus, this analysis can **not** "be performed with any polynucleotide". Second, the Examiner once again is clearly confusing the requirements of a **specific** utility with a **unique** utility. The fact that a small number of other nucleotide sequences could be used to map the protein coding regions in this specific region of chromosome 11 does not mean that the use of Appellants' sequence to map the protein coding regions of chromosome 11 is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

Regarding the utility requirements under 35 U.S.C. § 101, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)). Thus, based on the relevant case law, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, While Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent

examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit** L), 5,654,173 (**Exhibit** M), and 5,552,281 (**Exhibit** N; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit** O; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants understand that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1 and 5-9 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in Section VIII(A) concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have

determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1 and 5-9 have been shown to have "a specific, substantial, and credible utility", as detailed in Section VIII(A) above, the present rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:7.

5. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence of SEQ ID NO:7; and

(b) hybridizes to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. (Previously Presented) An isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:6.

7. (Previously Presented) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

8. (Previously Presented) The recombinant expression vector of claim 7, wherein said isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:6.

9. (Previously Presented) A host cell comprising the recombinant expression vector of claim 7.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1 and 5-9 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

December 2, 2003
Date

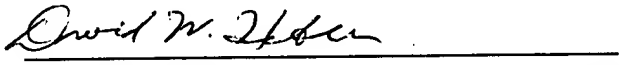

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TABLE OF AUTHORITIES

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